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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,860	06/30/2006	Ariel G. Notcovich	27396U	3336

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THE NATH LAW GROUP
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EXAMINER	
LAM, ANN Y	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,860	NOTCOVICH ET AL.	
	Examiner	Art Unit	
	ANN Y. LAM	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-37,39 and 41-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-37, 39 and 41-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

As a preliminary matter, the finality of the previous Office action of November 13, 2009 is hereby withdrawn. It is noted that Applicant's response of August 21, 2009 was not intended to be a response to the nonfinal action of August 6, 2009 but was submitted only to amend the specification. Thus, the final rejection of November 13, 2009 was provided in error on the assumption that the response of August 6, 2009 was a response to the nonfinal action of August 6, 2009. Applicant's response of February 12, 2010 should have properly been entered as a response to nonfinal as opposed to an after final response. Prosecution has therefore been reopened. The finality of the Office action of November 13, 2009 is withdrawn. It is noted however, that this present Office action is made final for the reasons set forth further below.

Claim Objections

Claims 29 and 37 are objected to because of the following informalities.

In claim 29, line 3, "member" should be --members--, since there needs to be more than one member for there to be simultaneous adsorbing. Likewise with line14, "member" should be --members--.

For the same reason, in claim 37, lines 8 and 12, respectively, "member" should be –members--.

Appropriate correction is required.

Applicant has argued that "simultaneous" in the claims can encompass the first and second binding members simultaneously provided. However, Examiner does not see any support for this interpretation in the specification. To the contrary, all the disclosed embodiments provide the first binding member and second binding member sequentially with each other, and there is no support as to how the first and second binding members are provided or absorbed at the same time.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 29-31, 33, 35-37, 41, 42 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Winkler et al., 5,384,261, in view of Ivarsson, 6,493,097, and further in view of Lambert, 20060210984.

Winkler et al. teach the synthesis of an array of different peptides in selected regions of a substrate. Such substrates having the diverse sequences formed thereon may be used in, for example, screening studies to evaluate their interaction with receptors such as antibodies. For example, in preferred embodiments the invention

provides for screening of peptides to determine which if any of a diverse set of peptides has strong binding affinity with a receptor and, in most preferred embodiments to determine the relative binding affinity of various peptides with a receptor of interest such as an antibody. Column 6, lines 6-20.

In operation, the substrate may be provided with appropriate linker molecules on the surface thereof. Thereafter, the surface is provided with protected surface active groups. Column 9, lines 15-28.

Thereafter, the channel block and the substrate are brought into contact forming fluid-tight channels bounded by the grooves in the channel block and the substrate. When the channel block and the substrate are in contact, a protective group removal agent is, thereafter, directed through a first selected channel or group of channels by placing the pipettor on the flow inlet of the selected channel and, optionally, the vacuum source on the outlet of the channel. In the case of, for example, TBOC protected amino acids, this protective group removal agent may be, for example, trifluoroacetic acid (TFA). This step is optionally followed by steps of washing to remove excess TFA with, for example, dichloromethane (DCM). Column 9, lines 29-42.

Thereafter, a first amino acid or other monomer A is directed through the first selected flow channel. Preferably this first amino acid is also provided with an appropriate protective group such as TBOC, FMOC, nitroveratryloxycarbonyl (NVOC) or the like. This step is also followed by appropriate washing steps. These steps of deprotection/coupling are concurrently with or thereafter repeated for additional

channels parallel to the first channel(s) which are to be provided with the same or different monomers. Column 9, lines 43-52.

Thereafter, the substrate and the channel block are separated and, optionally, the entire substrate is washed with an appropriate material to remove any unwanted materials from the points where the channels contact the substrate. Column 9, lines 53-57.

The substrate and/or block is then, optionally, washed and translated and/or rotated with the stage. In preferred embodiments, the substrate is rotated 90 degrees from its original position, although some embodiments may provide for greater or less rotation, such as from 0 to 180 degrees. Column 9, line 58 – column 10, line 3.

The steps of deprotection, and coupling of amino acids or other monomers is then repeated, resulting in the formation of an array of polymers on the surface of the substrate. For example, a monomer B may be directed through selected flow channels, providing the polymer AB at intersections of the channels formed by the channel block in the first position with the channels formed by the channel block after 90-degree rotation. Column 10, lines 4-11.

According to preferred embodiments, the array of polymer sequences is utilized in one or more of a variety of screening processes. For example, the substrate is then exposed to a receptor of interest such as an enzyme or antibody. According to preferred embodiments, the receptor is labelled with fluorescein, or otherwise labelled, so as to provide for easy detection of the location at which the receptor binds. According to some embodiments, the channel block is used to direct solutions

containing a receptor over a synthesized array of polymers. For example, according to some embodiments the channel block is used to direct receptor solutions having different receptor concentrations over regions of the substrate.
Col 11, line 17-35.

It is also disclosed that diverse polymer sequences are preferably synthesized on a single substrate. By synthesizing the diverse polymer sequences on a single substrate, processing of the sequences to evaluate their characteristics, such as relative binding affinity, is more easily conducted. By way of example, when a variety of peptide sequences are to be evaluated to determine their relative binding affinity to a receptor, the entire substrate and, therefore, all or a group of the polymer sequences may be exposed to an appropriately labelled receptor and evaluated simultaneously. Column 6, lines 21-31.

The invention allows for coupling of additional monomer in a polymer, and that monomers may be introduced concurrently through the channels and thus only a single process step is required to perform two coupling steps simultaneously.
Column 6, lines 50-66.

Thus as to claims 29, 33 and 37, Winkler disclose activating (providing a deprotector) through the channels, simultaneously adsorbing first binding members through the channels, and deactivating (providing another protective group) and simultaneously providing second binding members through the channels. Also disclosed is using the channel block to direct receptor solutions having different receptor concentrations over regions of the substrate (col. 11, line 17-35). Given that

different solutions are provided through the different channels, as discussed further above, it is understood that the different concentrations are provided in the different channels.

Applicant also claims that the plurality of bindings carried out do not necessitate a regeneration step. It is disclosed in Applicant's specification in paragraph 0006 that as is known in the art and in commercially available devices, a standard kinetic binding interaction measurement includes washing and regeneration of the probe. That is, the second binding member (target) is removed so that another concentration of the target is contacted with the probe. Using the Winkler device as discussed above does not necessitate a regeneration step in order to provide the different concentrations of analyte since they are provided through the different channels and detected simultaneously.

Applicant also claims simultaneously obtaining one or more kinetic parameters indicative of a binding reaction between the first binding member and the second binding member at each of the plurality of microspots to produce a kinetic analysis of the binding. Kinetic measurements are not discussed by Winkler et al.

However, Ivarrson teach an improved method that allows for each sensor zone to be monitored simultaneously (column 7, line 60 – column 18, line 7.) Ivarrson also teaches that instead of measuring and presenting surface concentrations, it is possible to measure and present surface concentration changes, surface refractive indexes, surface refractive index changes, surface thicknesses and surface thickness changes. The amounts of sample species bound or adsorbed to the different sensor spots or

subzones may be related to each other by analytical software. The time relation of the refractometric images makes it possible to obtain via further image data processing mass distribution kinetic data for, e.g., specific sample binding/desorption, sample displacement along the sensor surface, or for the separation process. Column 23, lines 53-64.

It is also disclosed by Ivarrson that types of optical principles used may be for example surface plasmon resonance (SPR), Brewster angle (both internal and external), ellipsometry angle (both internal and external), critical angle, and frustrated total reflection waveguide resonance. Column 9, lines 40-48.

While these types of optical detection are not specifically disclosed by Winkler et al, the skilled artisan would have been suggested to combine the teachings since Winkler et al. do not limit the types of detection that can be used, and Ivarrson disclose a technique that is useful for detecting different sensor spots simultaneously.

It is noted that Winkler et al. teach that screening will be performed by, for example, separating or cutting two halves of the device, enabling screening by, for example, contacting with a fluorescein labeled antibody, or the like followed by photodetection. Column 12, lines 29-32. Thus the skilled artisan is suggested to utilize known photodetection techniques, such as that disclosed by Ivarrson, that provides the benefit of simultaneous analysis, such as kinetic analysis, of different sensor zones. Given the improvements of Ivarrson, the skilled artisan would have had reasonable expectation of success in providing such improvements to the Winkler et al. invention to allow for simultaneous analysis in the different sensor zones..

Applicant further claims simultaneously obtaining reference data from a plurality of interspots, each of the microspots located at a surface between at least two or more microspots (interpreted to mean that the reference data spots are between spots with the first and second binding member).

This is disclosed by Lambert in disclosing a microassay chip functionalized with at least one analyte reaction spot, and at least one, and preferably at least two homologous calibration reaction spots arranged in a line (column) perpendicular to the flow of reagent across the surface of the chip, with said at least one analyte reaction spot being arranged in a line (row) with at least one of the calibration reaction spots such that the analyte reaction spot and the calibration reaction spot are parallel with the flow of reagent across the surface of the chip. In a more preferred embodiment, the microassay chip will include a plurality of calibration reaction spots arranged in a series of at least one and preferably at least two or more columns, each column comprised of a homologous population of calibration reaction spots, each calibration reaction spot comprised of preferably peptide nucleic acids, and each of said columns being comprised of spots of a different population of nucleic acid molecules, preferably peptide nucleic acids. See paragraph 0029. The invention is useful in proteomics for simultaneous analysis of thousands of biomolecular interactions on the surface of the microchip inserted in a flow cell cartridge and provides for normalizing or calibrating for variations in a signal intensity of binding reactions due to variations in reagent flow rate over the surface of the chip that occur as a result of the contact between the flow stream and the surfaces of the flow cell cartridge (paragraph 0002). Various techniques

may be used to detect the binding interaction, including surface plasmon resonance (SPR), (paragraph 004 and 0032.)

It would have been obvious to one of ordinary skills in the art at the time the invention was made to modify the invention of Winkler et al. to provide calibration spots in a line between lines of analyte reaction spots because it provides for the advantage of normalizing or calibrating for variations in a signal intensity of binding reactions as taught by Lambert. Providing such a pattern with alternating multiple lines of analyte reaction spots and calibration spots meets the claimed limitation of a plurality of interspots located at a surface between at least two or more microspots. Simultaneous analysis is also disclosed by Lambert (paragraph 002), and the skilled artisan would have recognized the benefits of convenience and efficiency of performing simultaneous reactions. The skilled artisan would have had reasonable expectation of success because both Winkler et al. and Lambert disclose patterns of reaction spots in a flow cell.

As to claim 30, SPR detection or Brewster angle reflectometry is disclosed by Ivarrson as discussed above (Ivarrson, column 9, liens 40-48.)

As to claims 31 and 43, the types of detection may be SPR as discussed above, and the parameter may be reflectance changes (Ivarrson, see for example, column 9, lines 1-9.)

As to claim 35, the deactivating step may be the washing step. As disclosed by Winkler et al, the substrate and the channel block are separated and, optionally, the entire substrate is washed with an appropriate material to remove any unwanted

materials from the points where the channels contact the substrate. Column 9, lines 53-57.

As to claim 36, obtaining reference data from a region of the surface not included in a microspot (i.e., another microspot used for control purposes) is discussed above regarding Lambert.

As to claim 41, forming a second channel perpendicular to the first channel is discussed above by Winkler et al.

As to claims 42 and 46, a probe array is produced as discussed above regarding Winkler.

Claims 32, 44 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Winkler et al., 5,384,261, in view of Ivarsson, 6,493,097, and further in view of Lambert, 20060210984, as applied to claim 29 above, and further in view of Natesan et al., 20020048792.

While Ivarsson teaches kinetic analysis in general as discussed above, there is no specific disclosure that the assay is to determine dissociation constant. Natesan et al. however teach in paragraph 0113 that a number of well-characterized assays are available for determining binding affinity, usually expressed as dissociation constant for DNA-binding proteins and the cognate DNA sequences to which they bind. While Ivarsson discloses only in general kinetic analysis, the skilled artisan would have the

knowledge to analyze kinetic parameters such as dissociation constants as such is understood in the art, as shown by Natesan et al.

Claims 34 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Winkler et al., 5,384,261, in view of Ivarsson, 6,493,097, and further in view of Lambert, 20060210984, as applied to claims 29 and 37 above, and further in view of Siddigi et al., 5,541,113.

While Ivarrson disclose a sensor surface such as gold or silver, for SPR detection technique (column 20, lines 40-45), Ivarrson is silent as to formation of the probes on the sensor. Thus, there is no disclosure of activating the surface by producing an electric field over the microspot.

Siddigi et al. however disclose that it is known that an electric field induces certain chemical reactions (col. 1, lines 51-56.) While the disclosure refers to a chemical reaction that can be detected, rather than for immobilizing a probe, the skilled artisan would have recognized that an electric field would induce similar reactions in certain ligands that may be of interest in order to cause a reaction for immobilization purposes, and thus use of an electric field to induce binding in the invention of the combination of the teachings of Winkler et al. and Ivarsson would have been obvious.

Response

Applicant's arguments and the affidavit filed February 12, 2010 have been considered and are found persuasive as to the Malmqvist et al. device not being capable of kinetic analysis where there is a concentration gradient in the laminar flow. It is noted that Applicant's arguments and the affidavit concern kinetic analysis of different concentration in a *laminar* flow in the *same* channel. It is noted that the cited references in the present grounds for rejection do not rely on laminar flow, nor different concentrations of analytes in the same channel, but rather in different channels.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANN Y. LAM whose telephone number is (571)272-0822. The examiner can normally be reached on Mon.-Thurs. 9-7:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ann Y. Lam/
Primary Examiner, Art Unit 1641